Infective Endocarditis

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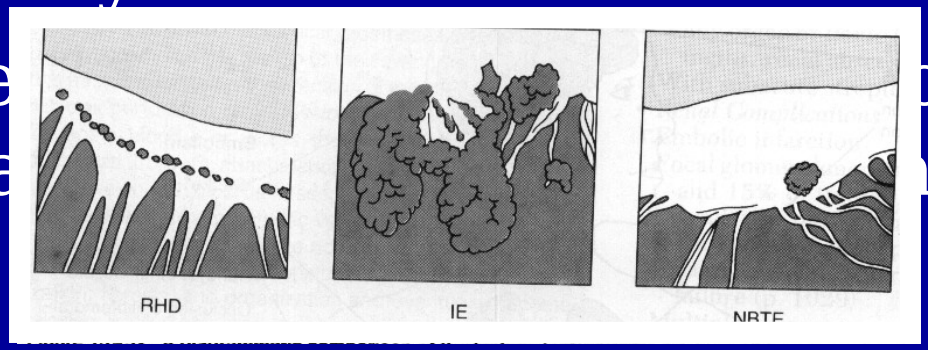
IE: More than a nostalgic disease.

- “One of the most serious of all infections.”*
  - Is uniformly fatal if untreated.
  - Continues to have a high case fatality rate even in antibiotic era.
    - 4th leading cause of life-threatening ID.
- Incidence is increasing.

* Pathologic Basis of Disease. Cotran, Kumar, Robbins. 4

Terminology:
SBE, IE, ABE, NVE, NBTE, or PVE?

- "Infectious endocarditis" now preferred…
  - subacute vs. acute is arbitrary and antiquated.
  - etiology may be fungal, bacterial, possibly viral
  - "Infe… om mara… tic, etc.

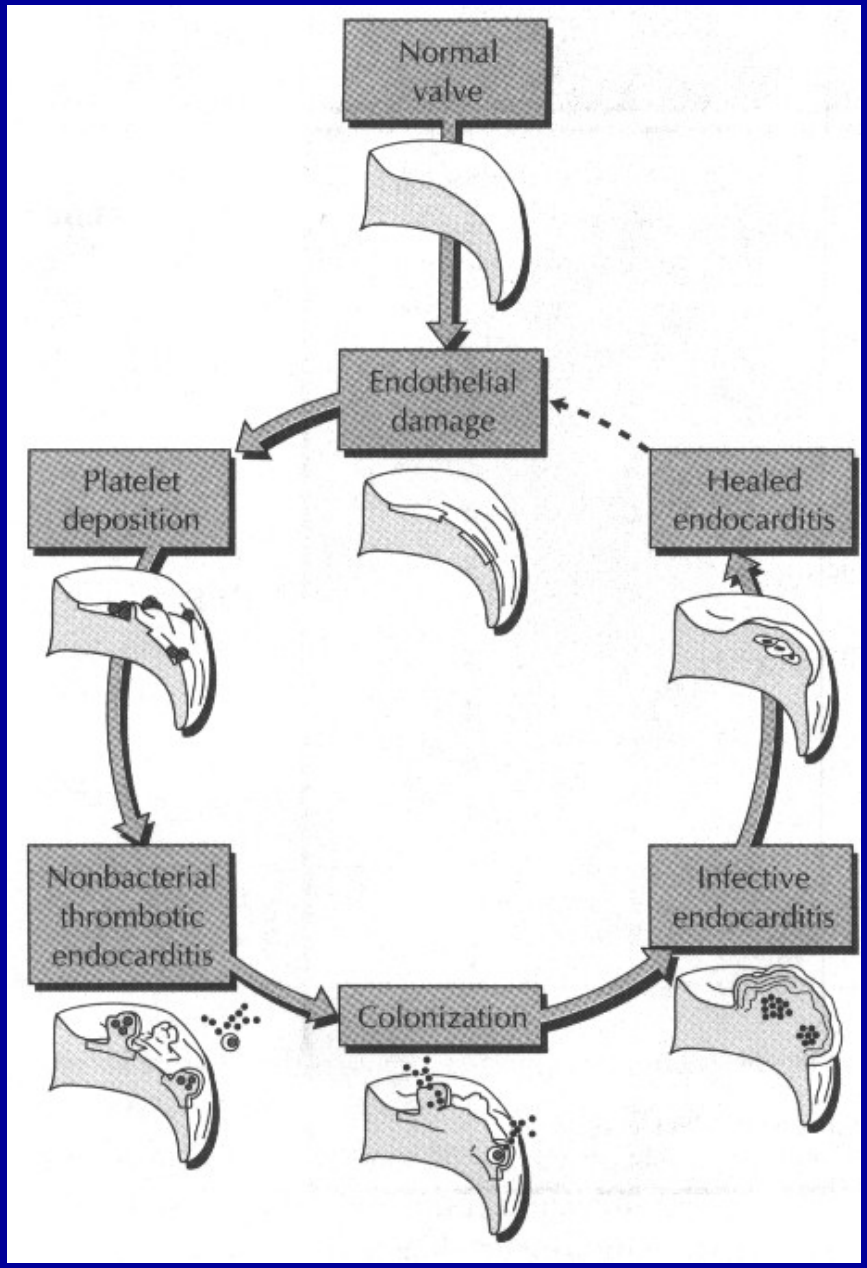


Epidemiology

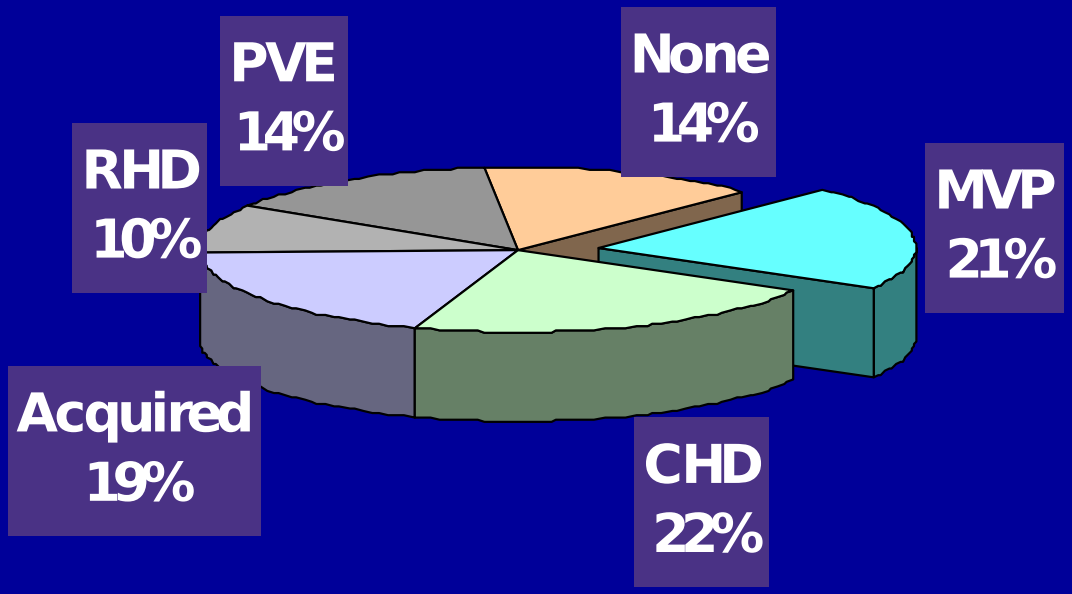
- Exact incidence difficult to measure.
  - Estimated at 0.16 - 5.4 cases/1000 admissions.
  - Is increasing as the at-risk population grows.
- Age distribution is changing.
  - mean age of patient is up to 55 years.
- Male:Female = 2-9:1
- Uncommon in pregnancy

Epidemiology

- Severe kidney disease
- Diabetes
- IVs or skin disease
  - (skin flora)
- Flossing (borderline)
  - (dental flora)
- Not most procedures


Normal valve
Endothelial damage
Platelet deposition
Healed endocarditis
Nonbacterial thrombotic endocarditis
Infective endocarditis
Colonization

Predisposing Conditions

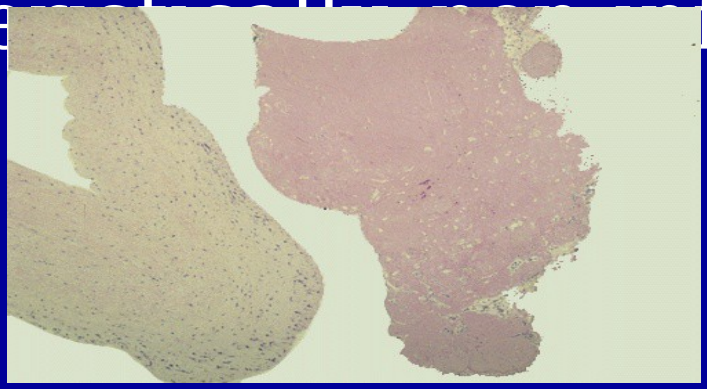


IV drug users and nosocomial cases excluded.

Strom BL, Abrutyn E, Berlin JA, Kinman JL, Feldman RS, Stolley PD, et al. Ann Intern Med. 1998;129:761-9.

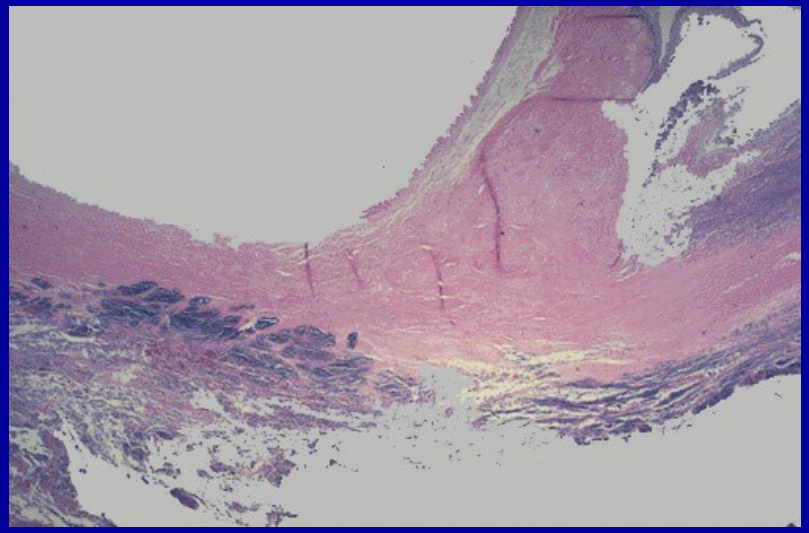
Nonbacterial Thrombotic Endocarditis

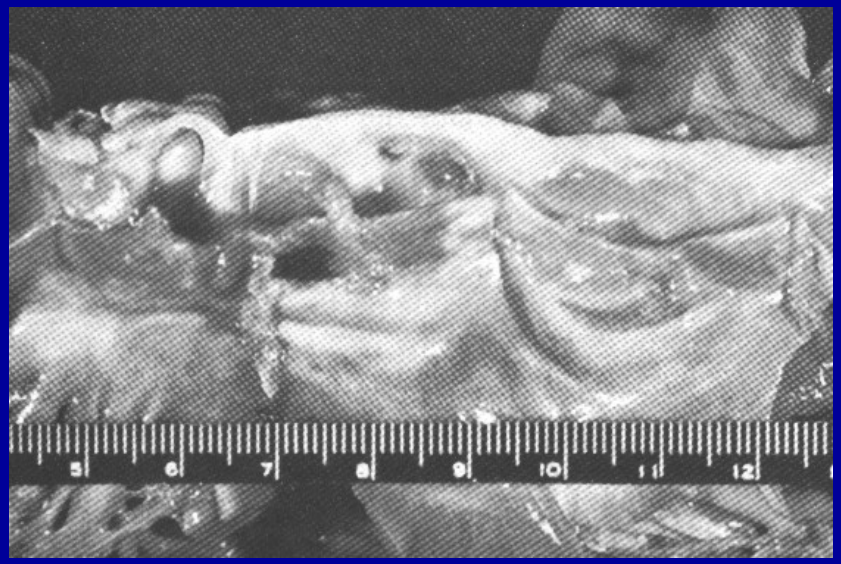
- Sterile platelet-fibrin deposits
- Occur at sites of eddy currents or jet streams created by pre-existing cardiac disease
- Create the “soil” for bacterial deposition.
- Characte flammatory



Infection

Growth of vegetation by platelet-fibrin deposition yields a sanctuary for bacteria.





Microbiology

sx's<60 d post

	NVE (%)	Intravenous Drug Abusers (%)	Early PVE (%)	Late PVE (%)
Streptococci	65	15	10	35
Viridans, alpha-hemolytic	35	5	<5	25
S. bovis (group D)	15	<5	<5	<5
S. faecalis (group D)	10	8	<5	<5
Other streptococci	<5	<5	<5	<5
Staphylococci	25	50	50	30
Coagulase-positive	23	50	20	10
Coagulase-negative	<5	<5	30	20
Gram-negative aerobic bacilli	<5	15	20	15
Fungi	<5	5	10	5
Miscellaneous bacteria	<5	5	5	5
Diphtheroids, propionibacteria	<1	<5	5	<5
Other anaerobes	<1	<1	<1	<1
Rickettsia	<1	<1	<1	<1
Chlamydia	<1	<1	<1	<1
Polymicrobial infection	<1	5	5	5
Culture-negative endocarditis	5–10	5	<5	<5

Streptococci in IE

Organism
Alpha-hemolytic streptococci
S. sanguis
S. mitior, dextran negative
S. mitior, dextran positive
Unclassified
Nonhemolytic, non–group D
S. mutans
S. angiosus
S. salivarius
Group D
Enterococci
S. bovis
Pyogenic streptococci
Miscellaneous
Aerococci

Viridans Streptococci

- 30-65% of native valve endocarditis
- Normal oral commensals
- A group, composed of several species:
  - S. mitior, S. sanguis, S. mutans,etc.
  - Alpha-hemolytic, non-typable
- Typical agents of classic “SBE”

Other Streptococci

- *S. bovis*
  - Lancefield group D
  - Gut flora: associated with GI pathology
- *S. pneumonia*
  - 1-3% of cases of IE with predilection for AV
  - Usually, in those with immune suppression
    - DM and Ethanolism
- Group B Streptococci
  - Elderly with chronic disease

Enterococcus

- Normal inhabitant of GI tract.
- Frequently encountered in UTIs.
- Up to 40% of cases without identified underlying predisposition to IE.
- Difficult to treat due to drug resistance.

Staphylococci

- Coagulase Positive (Staph. aureus)
  - a major causative agent in all populations of IE
  - typically produces “acute” IE
    - fulminant, rapidly progressive with few immunologic signs.
    - CNS complications in 30-50%
- Coagulase Negative (Staph. epi, et al)
  - Major cause of PVE. 3-8% of NVE.

HACEK organisms

- Hemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella
- Gram negative inhabitants of the upper airways.
- Large vegetations, high likelihood of embolization.
- Slow growing: hold cultures for 3 weeks.
- Traditionally sensitive to beta lactams, now some produce beta lactamase.

Fungi

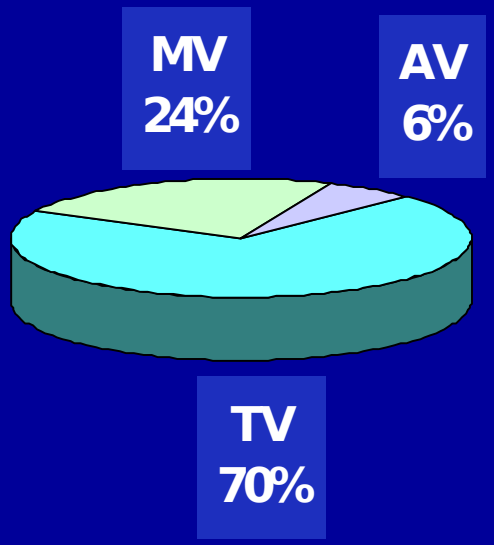
- Commonly encountered agents:
  - Candida, Torulopsis, Aspergillus
- Predispositions
  - Prosthetic valves
  - IVDA
  - Immunosupression
  - Hyperalimentation
  - Prolonged abx treatment
- Large vegetations and frequent embolic events.

Other Organisms

- Pseudomonas
- Brucella
- Diphtheroids
- Listeria
- Bartonella
- Coxsiella
- Chlamydia

IV Drug Users

- Accounts for 25% of cases of IE in US.
- 5:1 male:female
- Pre-existing valvular diseases uncommon.
- Variable microbiology.
- Mortality<10%.



Prosthetic Valve IE

- Affects 3% of prosthesis patients.
  - Highest risk in first 6 months post op.
- Accounts for 10-20% of all IE cases.
- Increased risk in…
  - Males
  - Blacks
  - Prolonged pump time
  - Multiple valve replacement

Prosthetic Valve IE

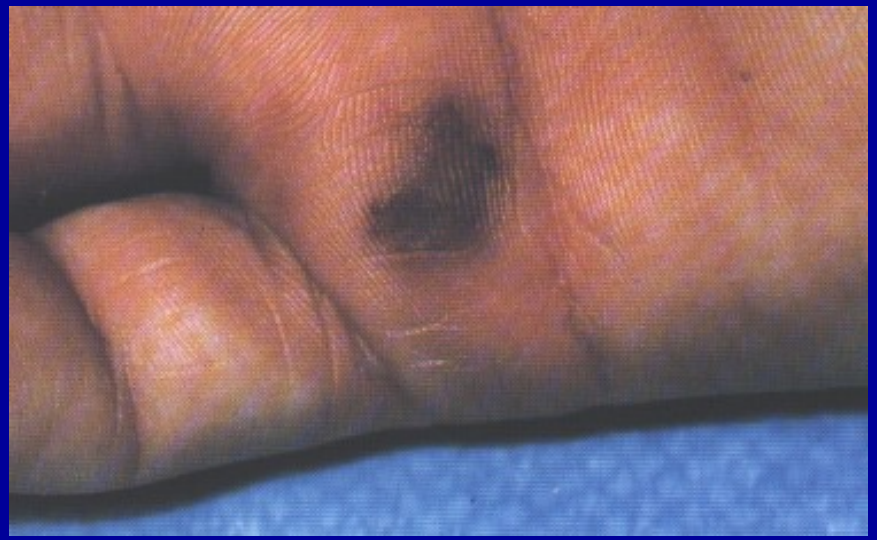
- “Early” (<2 months)-Staph epi
- “late” (after 2 months)- mimics NVE

Clinical Features

SYMPTOMS	PER CENT	SIGNS	PER CENT
Fever	80–85	Fever	80–90
Chills	42–75	Murmur	80–85
Sweats	25	Changing/new murmur	10–40
Anorexia	25–55	Neurological abnormalities†	30–40
Weight loss	25–35	Embolic event	20–40
Malaise	25–40	Splenomegaly	15–50
Dyspnea	20–40	Clubbing	10–20
Cough	25	Peripheral manifestation	
Stroke	13–20	Osler's nodes	7–10
Headache	15–40	Splinter hemorrhage	5–15
Nausea/vomiting	15–20	Petechiae	10–40
Myalgia/arthralgia	15–30	Janeway lesion	6–10
Chest pain*	8–35	Retinal lesion/Roth spot	4–10
Abdominal pain	5–15		
Back pain	7–10		
Confusion	10–20		

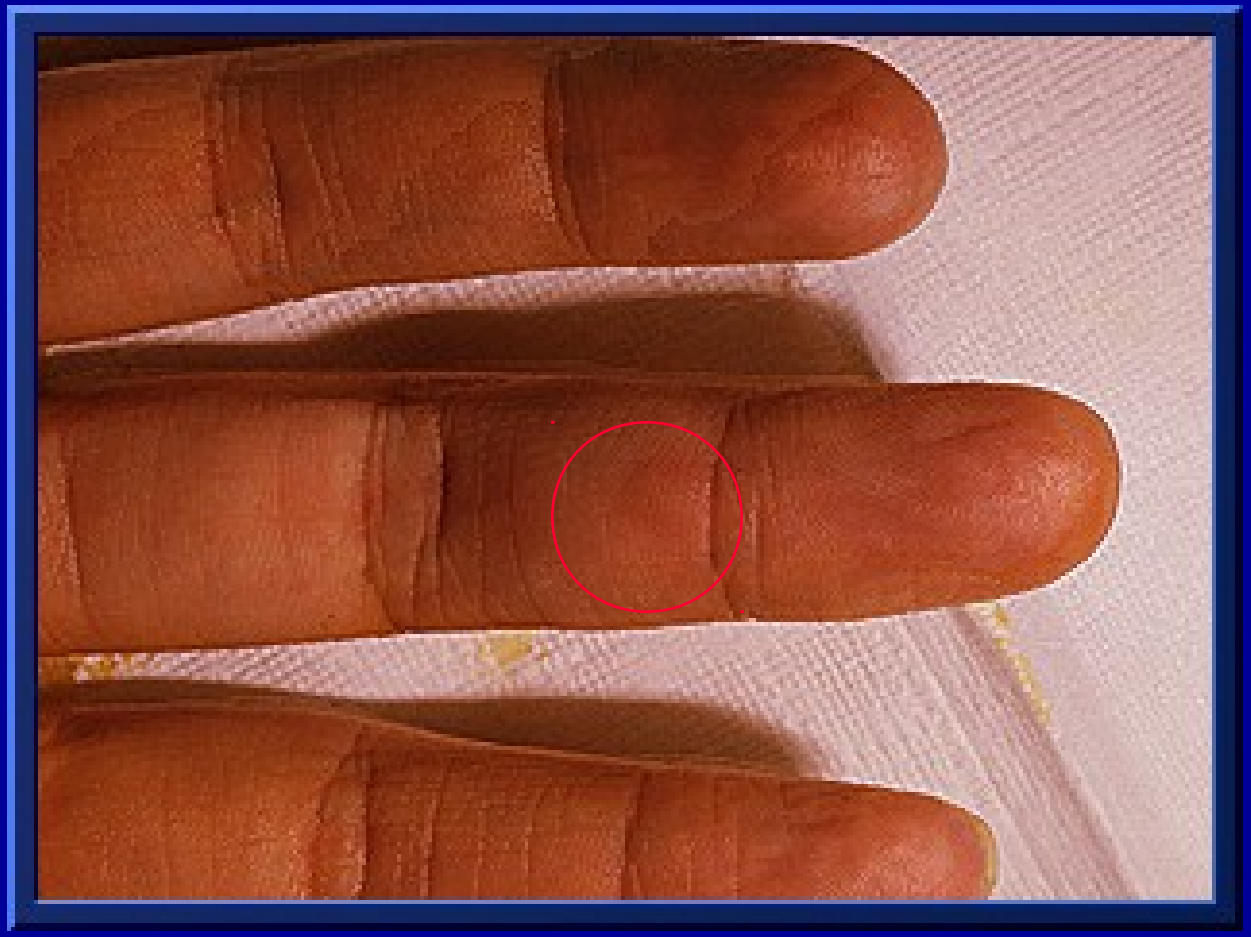
Peripheral Manifestations

- Janeway Lesions:
  - erythematous, macular, non tender.
  - septic emboli?



- Osler's Nodes:
  - Tender, subcutaneous nodules.
  - 4 P's:
    - Pink
    - Painful
    - Pea-sized
    - Pulp of the fingers/toes.
  - Immunologic

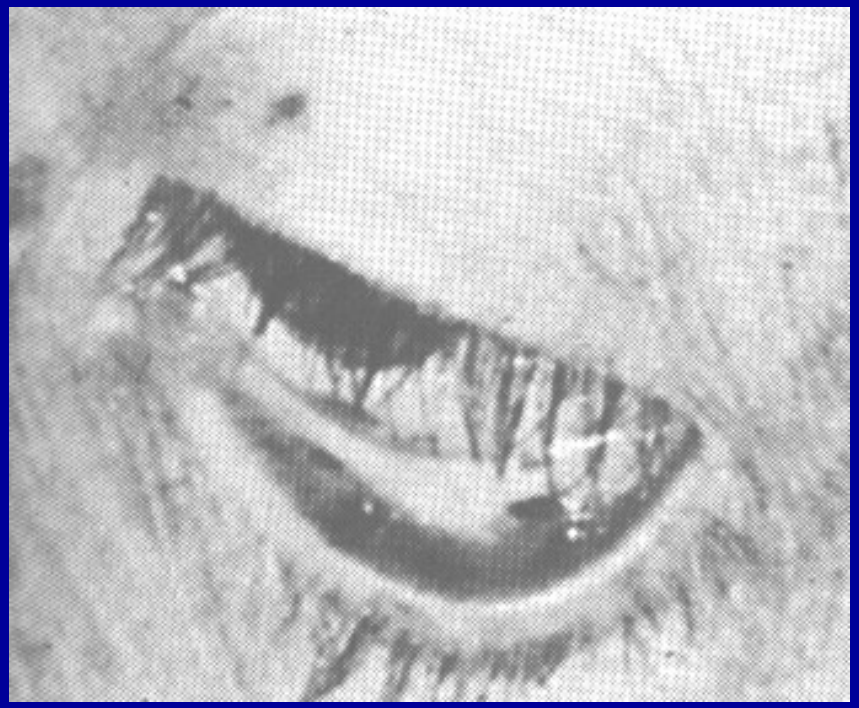
Osler’s Node



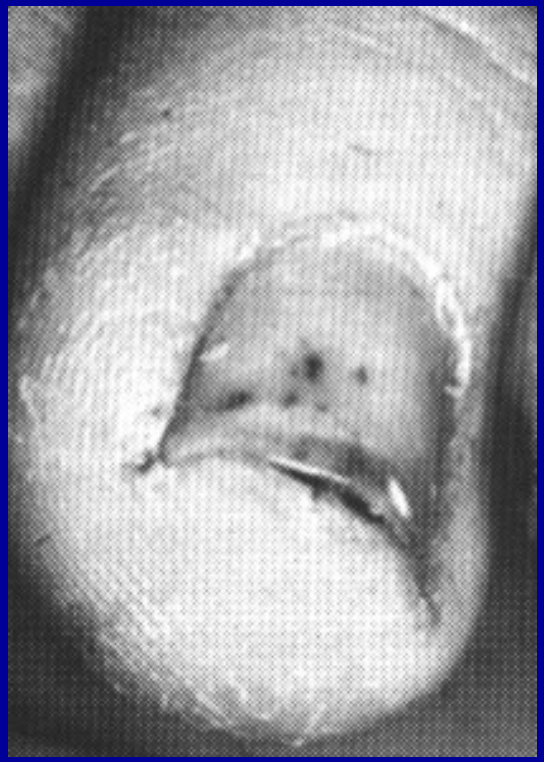
Bleeding

- Subungual (splinter) hemorrhage
- Conjunctival hemorrhage
- Retinal hemorrhage: Roth Spot

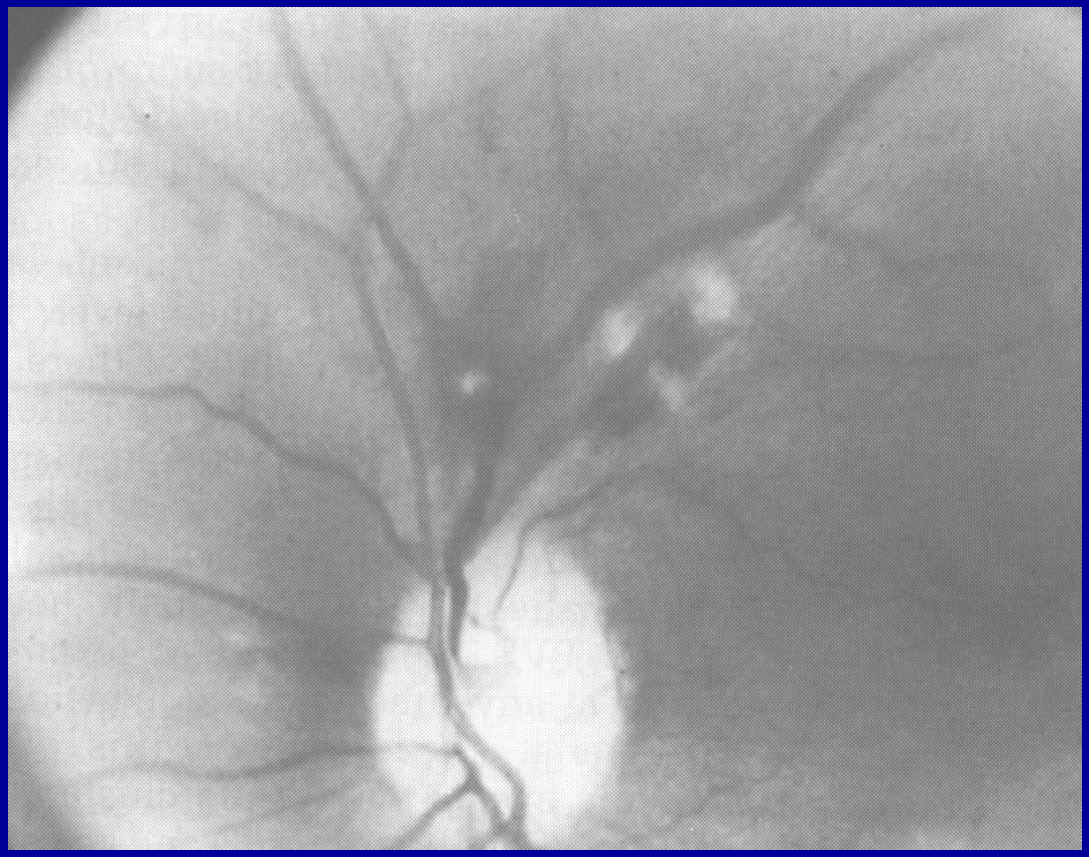
Conjunctival Petechiae



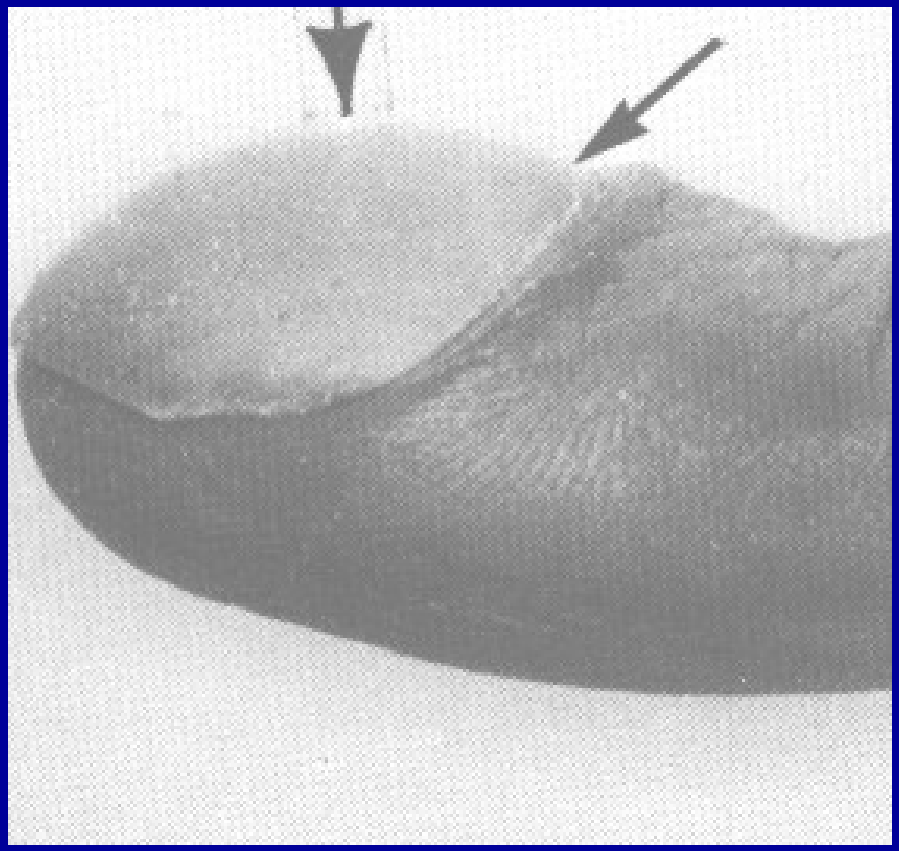
Splinter Hemorrhage



Roth Spot



Clubbing



Lab Investigations

- Anemia of Chronic Disease in 50-80%
- ESR “almost always” elevated.
  - May be normal in those with CHF.
- Urinalysis
  - gross or microscopic hematuria
  - casts in glomerulonephritis
  - bacteriuria and pyuria
- Elevated BUN and Creatinine
- Rheumatoid factor present in 50%

Diagnosis

- Frequently difficult to diagnose with certainty.
  - Highly variable and often non-specific presentation.
- Overdiagnosis and Underdiagnosis are common.

Diagnosis

- Classic Clinical Approach:
  - Von Reyn (Beth Israel) Criteria
    - Limitations:
      - No Use of Echo.
      - IVDA not identified as a predisposition
      - Lacks sensitivity for “acute” cases.
- Incorporation of Echo:
  - Durack (Duke) Criteria
    - Increases proportion of definite diagnoses.

Diagnosis-Duke Criteria

- Major:
- Persistently positive blood cultures
  - Typical organisms for IE
  - Persistent bacteremia
- Evidence of endocardial involvement
  - Positive ECHO
  - New valvular regurgitation

Diagnosis-Duke Criteria

- Minor:
- Predisposing heart condition
- Fever
- Vascular phenomena
- Immunologic phenomena
- Positive BC (not meeting major)
- Positive ECHO (not meeting major)

Diagnosis-Duke Criteria

- “Definite”:
- pathologic diagnosis
  - Micro-organisms or
  - Pathologic lesion (confirmed by histology)
- clinical diagnosis
  - 2 major criteria or
  - 1 major criterion plus 3 minor criteria or
  - 5 minor criteria

Diagnosis-Duke Criteria

- “Probable”:
  - Findings consistent with endocarditis but fall short of definite and
  - not rejected
- “Rejected”
  - Firm alternate diagnosis for manifestations or
  - resolution of manifestations <= 4 days antibiotics or
  - No pathologic evidence of IE at surgery or autopsy after 4 days therapy

“Echo should be done in all cases of suspected endocarditis.”

(This is not all patients with fever or positive bloo

Circulation 1997; 95: 1686-1784

Use of Echo in Diagnosis of IE

- Native Valves-ACC Guidelines:
  - Detection/characterization of valvular lesions
  - Detection of vegetations and characterization of lesions in patients with CHD
  - Detection of associated abnormalities
  - Reevaluation studies in complex IE
  - Evaluation of patients with high suspicion of culture-negative IE

Use of Echo in Diagnosis of IE

- Prosthetic Valves-ACC Guidelines:
  - Detection/characterization of valvular lesions
  - Detection of associated abnormalities
  - Reevaluation in complex IE
  - Evaluation of suspected IE and negative cultures
  - Evaluation of persistent fever without known source

Use of Echo in Diagnosis of IE

- TEE:
  - Prosthetic valves
  - Poor visualization on TTE and high suspicion
  - Detection of associated complications
  - Preoperative
  - Reevaluation in complex IE

Medical Management

- Tailor therapy to results of susceptibility testing.
- Use parenteral drugs.
- Plan for prolonged courses of abx.
  - Be vigilant for adverse drug effects.
- Use bactericidal agents.
- Synergistic combinations are useful.
- Monitor levels of aminoglycosides.

Persistent Fever on Appropriate Antibiotics

- Resistance
- Abscess:
  - local
  - distant
- Superinfection
  - Fungus

Culture Negative Endocarditis

- Most common cause is recent use of abx.
- Fastidious organisms
- Fungal
- Intracellular agents: Bartonella, chlamdia, viruses.
- Non-infectious (marantic)

Anticoagulation

"If anticoagulation is indicated fo
another reason it should be conti
Anticoagulation does not prevent
embolization due to IE."

ACC guidelines on Diagnosis and Management of Infective Endocarditis.

Class I Indications for Surgery

- Acute AR or MR with heart failure.
- Acute AR with tachycardia and early closure of the MV.
- Fungal endocarditis.
- Annular or aortic abscess.
- Sinus or aortic aneurysm.
- Persistent bacteremia and valve dysfunction
  - After 7-10 days of appropriate antibiotics.

Circulation. 98(18):1949-1984, 1998

Other Indications for Surgery

- Class IIa
  - Recurrent emboli after appropriate abx.
  - Agent with known poor response to abx (GNR) with valve dysfunction.
- Class IIb
  - Mobile vegetations >10 mm.
- Class III
  - Early infections of MV that can likely be repaired.
  - Persistent pyrexia and leucocytosis with negative blood cultures.

Circulation. 98(18):1949-1984, 1998

TABLE 5. Echocardiographic Features Suggesting Potential Need for Surgical Intervention*

Vegetation
Persistent vegetation after systemic embolization:
Anterior mitral leaflet vegetation, particularly with size >10 mm†
One or more embolic events during first 2 weeks of antimicrobial therapy†
Two or more embolic events during or after antimicrobial therapy†
Increase in vegetation size after 4 weeks of antimicrobial therapy†‡
Valvular dysfunction
Acute aortic or mitral insufficiency with signs of ventricular failure‡
Heart failure unresponsive to medical therapy‡
Valve perforation or rupture‡
Perivalvular extension
Valvular dehiscence, rupture, or fistula‡
New heart block‡
Large abscess, or extension of abscess despite appropriate antimicrobial therapy‡

Bayer AS, et al. Circ 98:25, 2936-48. 22/29 Dec 98

Features of High Risk for Complications

- Prosthetic cardiac valves
- Left-sided IE
- *Staphylococcus aureus*
- Fungal IE
- Prior IE

Features of High Risk for Complications

- Prolonged symptoms (>9 months)
- Cyanotic CHD
- Pulmonary-to-systemic shunts
- Poor response to antimicrobial therapy

Complications Occur in Over Half of All Cases

- Embolic: CNS and Peripheral
  - Ischemic
  - Hemorrhagic
  - Septic:
    - mycotic aneurysm
    - metastatic abscess
- Local invasive
  - Conduction abnormalities
  - Valvular dysfunction
  - CHF
- Glomerulonephritis

CHF

- High associated mortality
  - Accounts for 80-90% of IE deaths
- Leading indication for surgery
- More common with AV involvement
- More common with *Staph aureus*?
- Surgery is strongly indicated in most cases.
  - In-house death reduced from 51% to 9%.
  - Once CHF develops, surgery should be performed promptly.

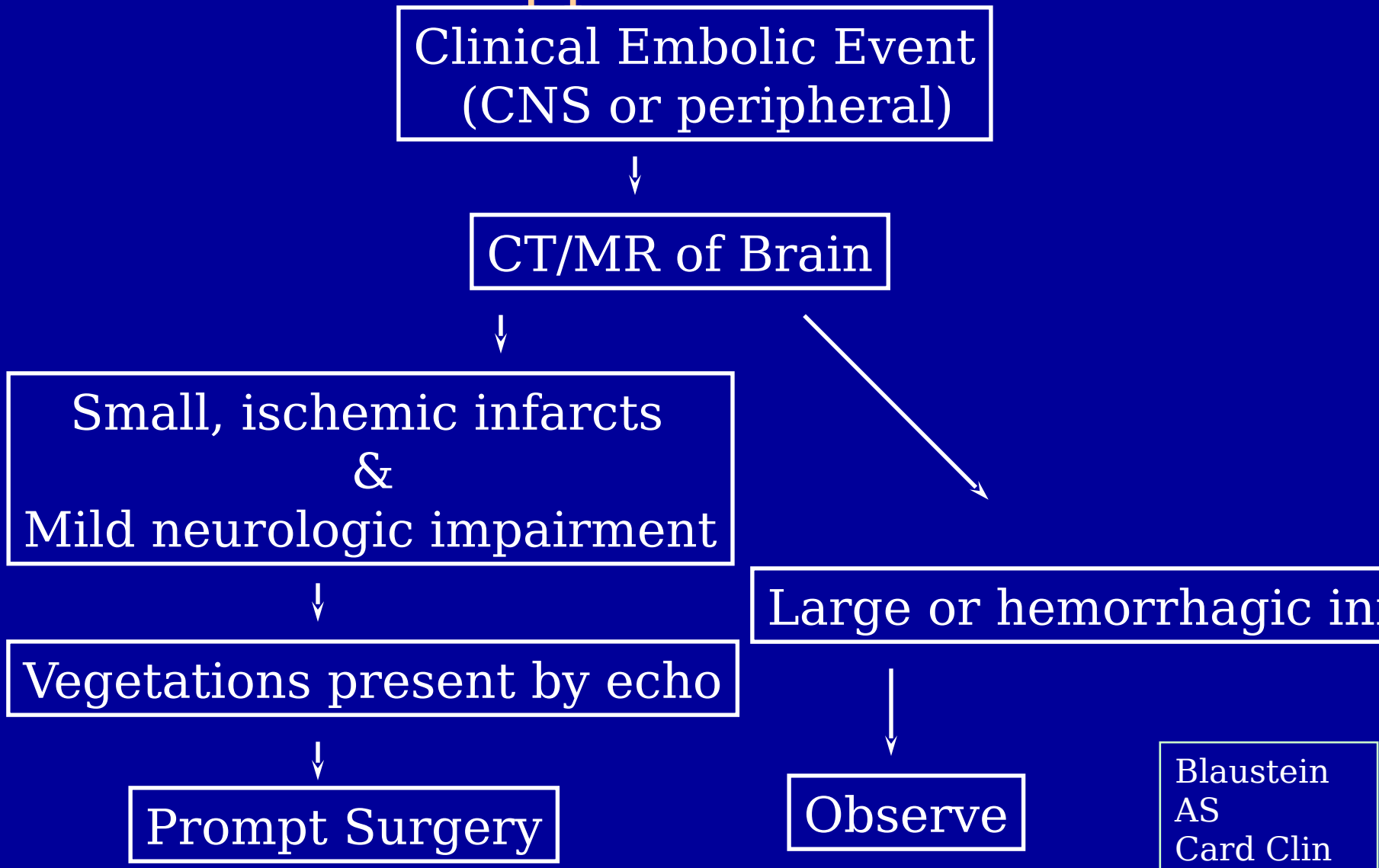
Embolic Events

- Occurs in 22-50% of cases.
- 65% of events occur in CNS
  - 90% of these in MCA distribution
  - Associated with high mortality
- Highest incidence with *S. aureus, Candida sp.,* and HACEK organisms.

Embolic Events

- Risk for embolism drops dramatically within two weeks of antibiotic therapy institution.
  - 13 to <1.2 events/1000 patient-days
  - MV disease > AV disease, AML disease the highest.
- Size of vegetation and embolic potential remain incompletely explained.

Embolic Events: an Aggressive Approach



Blaustein AS
Card Clin
14:3,1996

Mycotic Aneurysm

- 2-5% of all cerebral aneurysms
- More common in debilitated patients
- Suspect when encountered in…
  - Persistent fever
  - Pulsatile mass/erythema in peripheral regions
  - Headache, meningitis, neuro deficit for cerebral
- Surgery recommended whenever possible.

Periannular Extension of Infection

- 10-40% of all NVE
  - AV>TV
- 56-100% of all PVE
  - annulus is usually the primary site of infection
- May develop into fistulous tracts or shunts.
- New AV block has a PPV of 88%.
- Best diagnosed by TEE.
- Best surgical option is frequently the homograft.
  - Improved penetration of antibiotics.

Risk for Endocarditis	No. of Cases per 1000 Patient-Years
High	
Pulmonary atresia with ventricular septal defect	11.5
Tetralogy of Fallot with palliative systemic-to-pulmonary shunt	8.2
Aortic valve stenosis*	7.2
Pulmonary atresia*	6.4
Unoperated ventricular septal defect	3.8
Moderate to low	
Primum atrial septal defect with cleft mitral valve*	1.8
Coarctation of the aorta*	1.2
Complete atrioventricular septal defect*	1.0
Tetralogy of Fallot*	0.7
Dextrotransposition of the great arteries*	0.7
Ventricular septal defect*†	0.6
No documented risk	
Atrial septal defect*	0
Patent ductus arteriosus*	0
Pulmonic stenosis*	0

Prophylaxis

*After definitive surgical repair. For pulmonary atresia, this represents establishment of right ventricle to pulmonary artery continuity.

†All cases of endocarditis occurred either with a residual ventricular septal defect or with associated aortic valve anomalies including bicuspid aortic valve and aortic insufficiency. No cases of endocarditis occurred with closed ventricular septal defect in the absence of other anomalies.

Circulation. 96(1):358-366, 1997 July 1.

High Risk: Prophylaxis Recommended

- Prosthetic cardiac valves, including bioprosthetic and homograft valves
- Previous bacterial endocarditis
- Complex cyanotic congenital heart disease (eg, single ventricle states, transposition of the great arteries, tetralogy of Fallot)
- Surgically constructed systemic pulmonary shunts or conduits

Moderate Risk: Prophylaxis Recommended

- Most other congenital cardiac malformations (other than above and below)
- Acquired valvular dysfunction (eg, rheumatic heart disease)
- Hypertrophic cardiomyopathy
- Mitral valve prolapse with valvular regurgitation and/or thickened leaflets

Low Risk: Prophylaxis Not Recommended

- Isolated secundum atrial septal defect
- Surgical repair of atrial septal defect, ventricular septal defect, or patent ductus arteriosus
  - (without residua beyond 6 mo)
- Previous coronary artery bypass graft surgery
- Mitral valve prolapse without valvular regurgitation *

Low Risk: Prophylaxis Not Recommended

- Physiologic, functional, or innocent heart murmurs
- Previous Kawasaki disease without valvular dysfunction
- Previous rheumatic fever without valvular dysfunction
- Cardiac pacemakers (intravascular and epicardial) and implanted defibrillators

Prophylaxis Recommended

- Respiratory Tract
  - Tonsillectomy
  - Violation of respiratory mucosa.
  - Rigid bronchoscopy.
- Gastrointestinal Tract
  - Esophageal sclerotherapy or stricture dilation
  - ERCP
  - Billiary surgery
  - Violation of intestinal mucosa
- GU Tract
  - Prostate surgery
  - Cystoscopy
  - Urethral dilatation

Prophylaxis Not Recommended

- Respiratory Tract
  - ET intubation
  - Flexible bronchoscopy
  - PE tubes
- GI Tract
  - TEE
  - EGD

Prophylaxis Not Recommended

- GU Tract
  - Vaginal hysterectomy
  - Vaginal delivery
  - C - section
  - In uninfected tissue:
    - D and C/Ab
    - Urethral cath
    - Sterilization
    - IUDs
  - Circumcision

Antibiotic Prophylaxis

Situation	Agent	Regimen
Standard general prophylaxis	Amoxicillin	Adults: 2.0 g; children: 50 mg/kg orally 1 h before procedure
Unable to take oral medications	Ampicillin	Adults: 2.0 g IM or IV; children: 50 mg/kg IM or IV within 30 min before procedure
Allergic to penicillin	Clindamycin **or**	Adults: 600 mg; children: 20 mg/kg orally 1 h before procedure
	Cephalexin† or cefadroxil† **or**	Adults: 2.0 g; children; 50 mg/kg orally 1 h before procedure
	Azithromycin or clarithromycin	Adults: 500 mg; children: 15 mg/kg orally 1 h before procedure
Allergic to penicillin and unable to take oral medications	Clindamycin **or**	Adults: 600 mg; children: 20 mg/kg IV within 30 min before procedure
	Cefazolin†	Adults: 1.0 g; children: 25 mg/kg IM or IV within 30 min before procedure

IM indicates intramuscularly, and IV, intravenously.

*Total children's dose should not exceed adult dose.

†Cephalosporins should not be used in individuals with immediate-type hypersensitivity reaction (urticaria, angioedema, or anaphylaxis) to penicillins.

Antibiotic Prophylaxis

Situation	Agents*	Regimen†
High-risk patients	Ampicillin plus gentamicin	Adults: ampicillin 2.0 g IM or IV plus gentamicin 1.5 mg/kg (not to exceed 120 mg) within 30 min of starting procedure; 6 h later, ampicillin 1 g IM/IV or amoxicillin 1 g orally
		Children: ampicillin 50 mg/kg IM or IV (not to exceed 2.0 g) plus gentamicin 1.5 mg/kg within 30 min of starting the procedure; 6 h later, ampicillin 25 mg/kg IM/IV or amoxicillin 25 mg/kg orally
High-risk patients allergic to ampicillin/amoxicillin	Vancomycin plus gentamicin	Adults: vancomycin 1.0 g IV over 1-2 h plus gentamicin 1.5 mg/kg IV/IM (not to exceed 120 mg); complete injection/infusion within 30 min of starting procedure
		Children: vancomycin 20 mg/kg IV over 1-2 h plus gentamicin 1.5 mg/kg IV/IM; complete injection/infusion within 30 min of starting procedure
Moderate-risk patients	Amoxicillin or ampicillin	Adults: amoxicillin 2.0 g orally 1 h before procedure, or ampicillin 2.0 g IM/IV within 30 min of starting procedure
		Children: amoxicillin 50 mg/kg orally 1 h before procedure, or ampicillin 50 mg/kg IM/IV within 30 min of starting procedure
Moderate-risk patients allergic to ampicillin/amoxicillin	Vancomycin	Adults: vancomycin 1.0 g IV over 1-2 h complete infusion within 30 min of starting procedure
		Children: vancomycin 20 mg/kg IV over 1-2 h; complete infusion within 30 min of starting procedure

IM indicates intramuscularly, and IV, intravenously.
*Total children's dose should not exceed adult dose.
†No second dose of vancomycin or gentamicin is recommended.

Infective Endocarditis

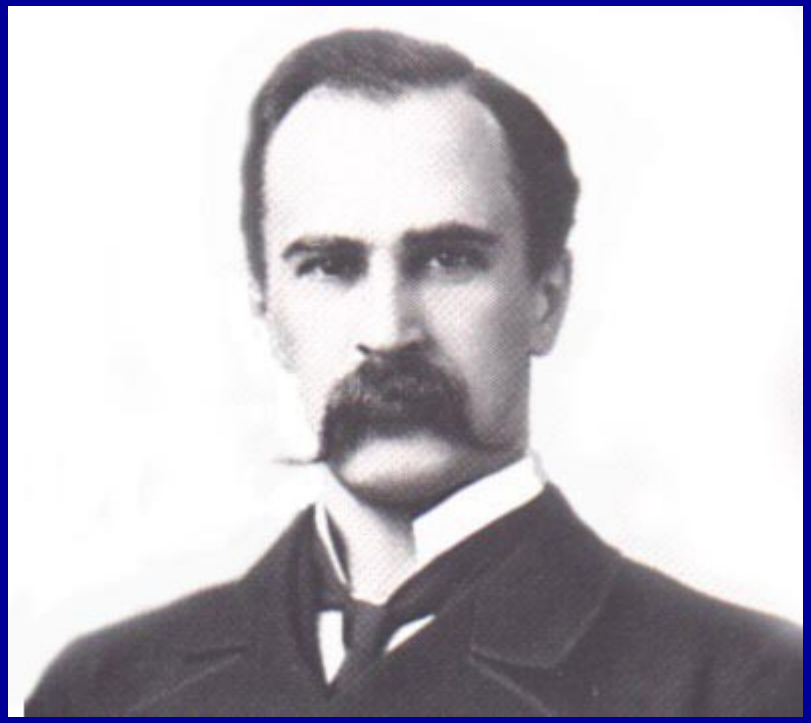
Questions?

Questions ?

“The practice of medicine is an art, not a trade; a calling, not a business; a calling in which your heart will be exercised equally with your head. Often the best part of your work will have nothing to do with potions and powders, but with the exercise of an influence of the strong upon the weak, of the righteous upon the wicked, of the wise upon the foolish.”

William Osler

Infective Endocarditis



19 January 1999

TABLE I

The von Reyn Criteria for Diagnosis of Infective Endocarditis*

Definite
- Direct evidence of infective endocarditis based on histology from surgery or autopsy, or on bacteriology (Gram's stain or culture) of valvular vegetation or peripheral embolus.

Probable
- (A.) Persistently postitive blood cultures† plus one of the following:
  - (1.) New regurgitant murmur, or
  - (2.) Predisposing heart disease‡ and vascular phenomena§
- (B.) Negative or intermittently positive blood cultures**plus three of the following:
  - (1.) Fever
  - (2.) New regurgitant murmur, and
  - (3.) Vascular phenomena

Possible
- (A.) Persistently positive blood cultures plus one of the following
  - (1.) Predisposing heart disease, or
  - (2.) Vascular phenomena
- (B.) Negative or intermittently positive blood cultures with all three of the following:
  - (1.) Fever
  - (2.) Predisposing heart disease, and
  - (3.) Vascular phenomena
- (C.) For viridans streptococcal cases only: at least two positive blood cultures without an extra-cardiac source, and fever

Rejected
- (A.) Endocarditis unlikely, alternative diagnosis generally apparent
- (B.) Endocarditis likely, empiric antibiotic therapy warranted
- (C.) Culture negative endocarditis diagnosed clinically, but excluded by postmortem

*Adapted from [1].

†At least two blood cultures obtained, with two of two positive, three of three positive, or at least 70% of cultures positive if four or more cultures obtained.

‡Definite valvular or congenital heart disease, or a cardiac prosthesis (excluding permanent pacemakers).

§Petechiae, splinter hemorrhages, conjunctival hemorrhages. Roth spots, Osler's nodes, Janeway lesions, aseptic meningitis, glomerulonephritis, and pulmonary, central nervous system, coronary or peripheral emboli.

**Any rate of blood culture positivity that does not meet the definition of persistently positive.

TABLE II

Proposed New Criteria for Diagnosis of Infective Endocarditis

Definite Infective Endocarditis
- Pathologic criteria
  - Microorganisms: demonstrated by culture or histology in a vegetation, *or* in a vegetation that has embolized, *or* in an intracardiac abscess, *or*
  - Pathologic lesions: vegetation or intracardiac abscess present, confirmed by histology showing active endocarditis
- Clinical criteria, using specific definitions listed in Table III
  - 2 major criteria, *or*
  - 1 major and 3 minor criteria, *or*
  - 5 minor criteria

Possible Infective Endocarditis
- Findings consistent with infective endocarditis that fall short of "Definite," but not "rejected."

Rejected
- Firm alternate diagnosis for manifestations of endocarditis, *or*
- Resolution of manifestations of endocarditis, with antibiotic therapy for 4 days or less, *or*
- No pathologic evidence of infective endocarditis at surgery or autopsy, after antibiotic therapy for 4 days or less

TABLE III

Definitions of Terminology Used in the Proposed New Criteria

Major Criteria
- Positive blood culture for infective endocarditis
  - Typical microorganism for infective endocarditis from two separate blood cultures
    - Viridans streptococci,* *Streptococcus bovis,* HACEK group, *or*
    - Community-acquired *Staphyloccus aureus* or enterococci, in the absence of a primary focus, *or*
  - Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis from:
    - (i) Blood cultures drawn more than 12 hours apart, *or*
    - (ii) All of three or a majority of four or more separate blood cultures, with first and last drawn at least 1 hour apart
- Evidence of endocardial involvement
  - Positive echocardiogram for infective endocarditis
    - (i) Oscillating intracardiac mass, on valve or supporting structures, *or* in the path of regurgitant jets, *or* on implanted material, in the absence of an alternative anatomic explanation, *or*
    - (ii) Abscess, *or*
    - (iii) New partial dehiscence of prosthetic valve, *or*
  - New valvular regurgitation (increase or change in pre-existing murmur not sufficient)

Minor Criteria

Predisposition: predisposing heart condition *or* intravenous drug use

Fever: ≥ 38.0°C (100.4°F)

Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions

Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth spots, rheumatoid factor

Microbiologic evidence: positive blood culture but not meeting major criterion as noted previously† *or* serologic evidence of active infection with organism consistent with infective endocarditis

Echocardiogram: consistent with infective endocarditis but not meeting major criterion as noted previously

HACEK = *Haemophilus* spp., *Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella* spp., and *Kingella kingae.*

*Including nutritional variant strains.

†Excluding single positive cultures for coagulase-negative staphylococci and organisms that do not cause endocarditis.

Pathologically Confirmed Cases n=69

	von Reyn Criteria			
	Probable	Possible	Rejected	Total (%)
New criteria				
Definite	32	19	4	55 (80)
Possible	3	3	8	14 (20)
Rejected	0	0	0	0 (0)
Total (%)	35 (51)	22 (32)	12 (17)	69 (100)

TABLE VIII

Comparison of Clinical Diagnoses in 336 Cases Evaluated for Diagnosis of Infective Endocarditis, Excluding Pathologically Proven Cases

	von Reyn Criteria			
	Probable	Possible	Rejected	Total (%)
New criteria				
Definite	65	59	11	135 (40)
Possible	6	56	87	149 (44)
Rejected	0	0	52	52 (15)
Total (%)	71 (21)	115 (34)	150 (45)	336 (100)

Additional Studies

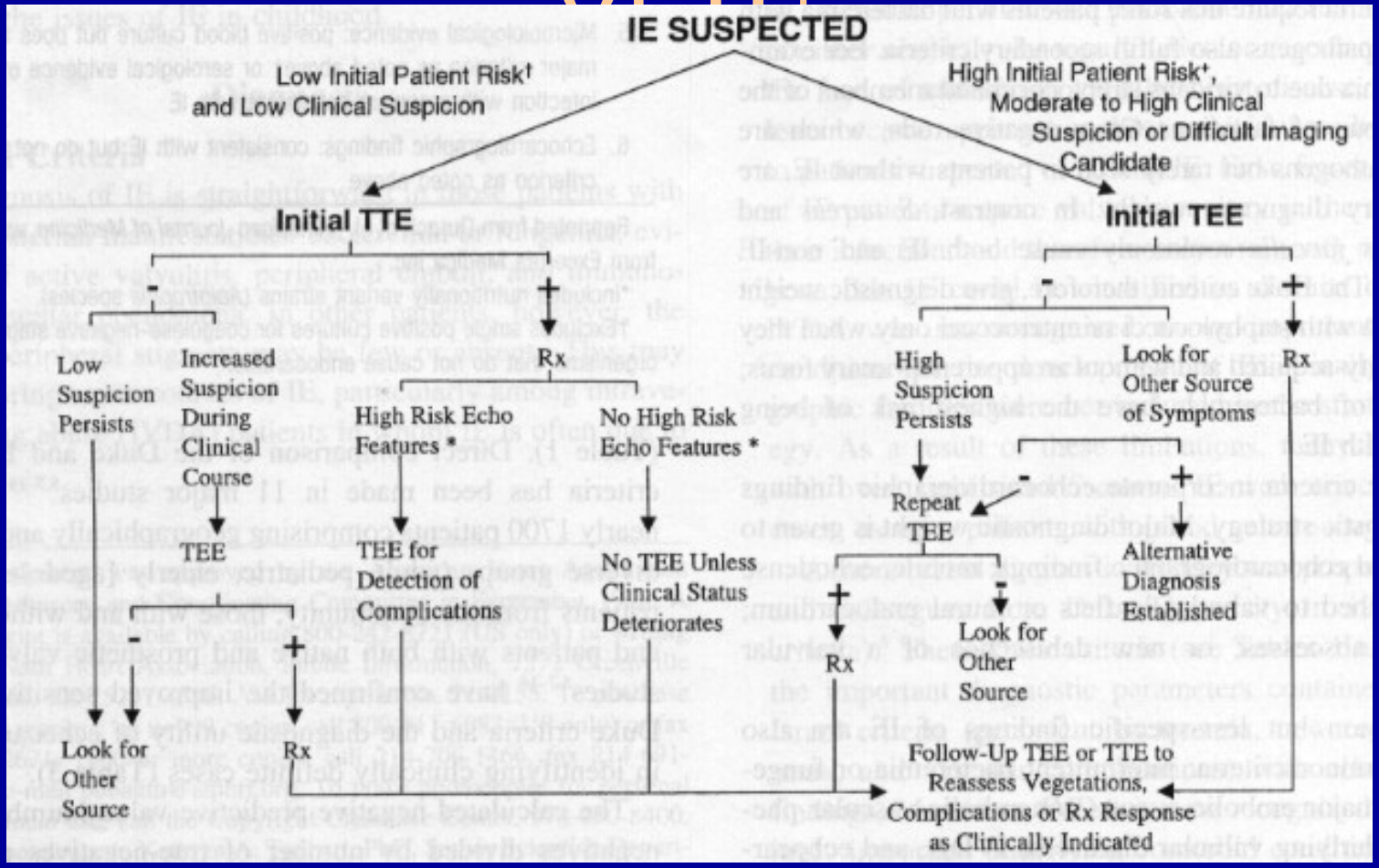
TABLE 3. Comparison of Duke Criteria With Beth Israel Criteria for the Clinical Diagnosis of IE: Summary of 11 Series[5,7–16]

Patients/Scheme	Clinically Definite	Probable	Possible	Rejected
Operated patients with surgically confirmed cases of endocarditis (n=286)*				
Beth Israel	N/A	47%	29%	24%
Duke	74%	N/A	26%	0
Nonoperated patients with clinically diagnosed cases of endocarditis (n=1395)				
Beth Israel	N/A	32%	30%	38%
Duke	55%	N/A	35%	10%

*Classified as if surgery had not been performed.

Bayer AS, et al. Circ 98:25, 2936-48. 22/29 Dec 98

Use of Echo in Diagnosis of IE



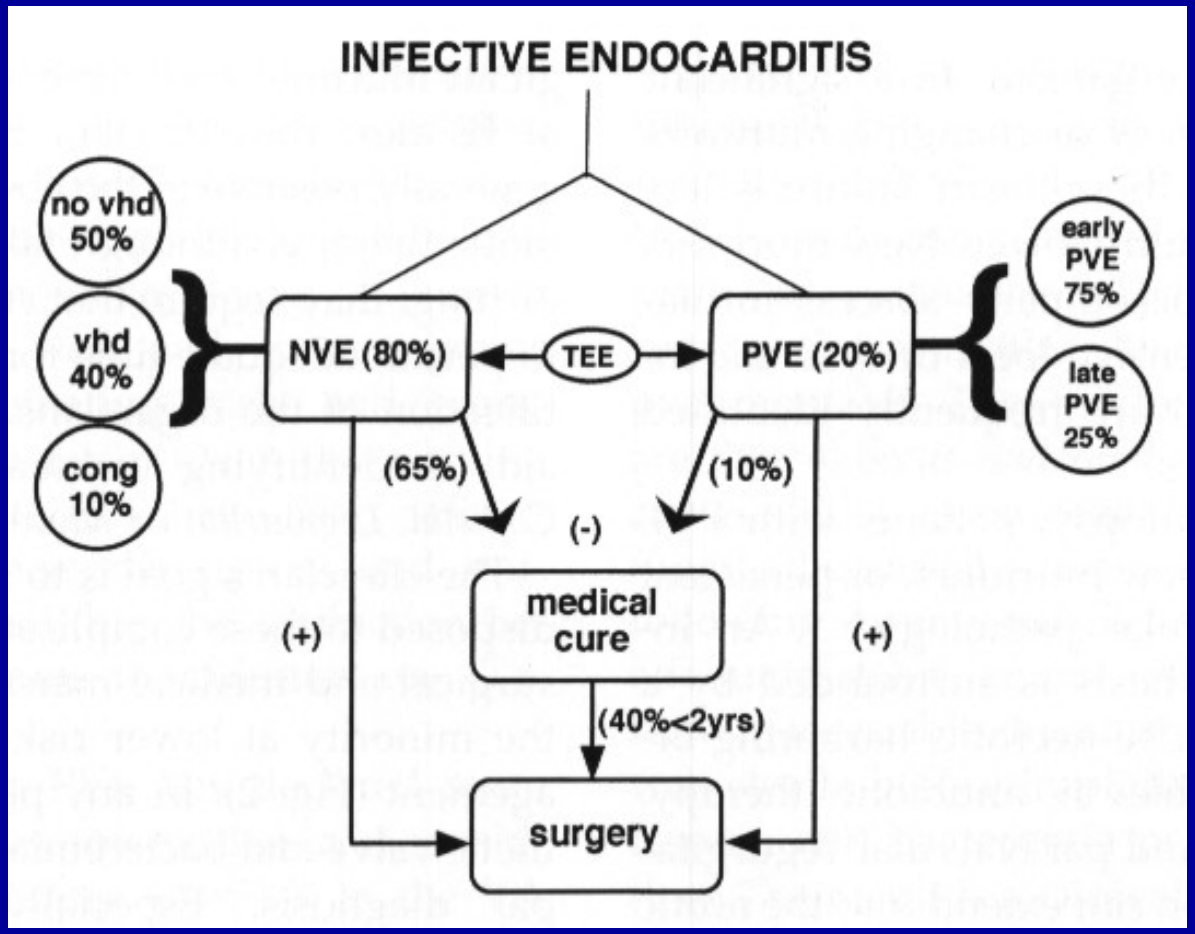
Bayer AS, et al. Circ 98:25, 2936-48. 22/29 Dec 98

	Indication	Class
1.	Detection and characterization of valvular lesions, their hemodynamic severity, and/or ventricular compensation.*	I
2.	Detection of vegetations and characterization of lesions in patients with congenital heart disease in whom infective endocarditis is suspected.	I
3.	Detection of associated abnormalities (eg, abscesses, shunts).*	I
4.	Reevaluation studies in complex endocarditis (eg, virulent organism, severe hemodynamic lesion, aortic valve involvement, persistent fever or bacteremia, clinical change, or symptomatic deterioration).	I
5.	Evaluation of patients with high clinical suspicion of culture-negative endocarditis.*	I
6.	Evaluation of bacteremia without a known source.*	IIa
7.	Risk stratification in established endocarditis.*	IIa
8.	Routine reevaluation in uncomplicated endocarditis during antibiotic therapy.	IIb
9.	Evaluation of fever and nonpathological murmur without evidence of bacteremia.	III

*Transesophageal echocardiography may provide incremental value in addition to information obtained by transthoracic imaging.

From the ACC/AHA Guidelines for the Clinical Application of Echocardiography.[2]

Management of IE



Antimicrobial Therapy for IE

The Sanford Guide to Antimicrobial Therapy

Gilbert DN, Moellering RC, Sande MA, eds. 28th ed. 1998.

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*	
		PRIMARY	ALTERNATIVE§
Heart *(continued)*			
Infective endocarditis—Native valve—empirical rx awaiting cultures	NOTE: Diagnostic criteria include evidence of continuous bacteremia (multiple posi ciency, definite emboli, and echocardiographic (transthoracic or transesophageal) e *22:276, 1996).*		
Valvular or congenital heart disease including mitral valve prolapse but no modifying circumstances	Viridans strep 30–40%, "other" strep 15–25%, enterococci 5–18%, staphylococci 20–35%	[(Pen G 20 mu qd IV, continuous or div. q4h) or (AMP 12 gm qd IV, continuous or div. q4h) + (nafcillin or oxacillin 2.0 gm q4h IV) + (gentamicin 1.0 mg/kg q8h IM or IV, not once daily dosing)]	Vanco 15 mg/kg[1] q12h IV (not to exceed 2 gm qd unless serum levels monitored) + gentamicin 1.0 mg/kg[1] q8h IM or IV
Infective endocarditis—Native valve—culture positive (Consensus opinion on treatment by organism: *JAMA 274*			
S. viridans, S. bovis with penicillin G MIC ≤0.1 μg/ml	S. viridans, S. bovis	(Pen G 12–18 mu/d IV, continuous or q4h x4 wks) OR (ceftriaxone 2.0 gm qd IV x4 wks) OR [(Pen G 12–18 mu/d IV, continuous or q4h x2 wks) PLUS (gentamicin 1 mg/kg q8h IV x2 wks)]	(Ceftriaxone 2.0 gm qd IV + gentamicin 1 mg/kg IV q8h both x2 wks.) If allergy pen G or ceftriaxone, use vanco 30 mg/kg/ d in 2 div. doses to 2 gm/d max. unless serum levels measured x4 wks
S. viridans, S. bovis with penicillin G MIC >0.1 to <0.5 μg/ml	S. viridans, S. bovis, nutritionally variant streptococci, tolerant strep[2]	Pen G 18 mu/d IV (continuous or q4h) x4 wks PLUS gentamicin 1 mg/kg q8h IV x2 wks	Vanco 30 mg/kg/d IV in 2 divided doses to max. 2 gm/d unless serum levels documented x4 wks
For S. viridans or S. bovis with Pen G MIC ≥1.0 and enterococci susceptible to amp/Pen G, vanco, gent. NOTE: Inf. Dis. consultation suggested	"Susceptible" enterococci, S. viridans, S. bovis, nutritionally variant streptococci	[(Pen G 18–30 mu/24h IV, continuous or q4h x4–6 wks) PLUS (gentamicin 1 mg/kg q8h IV x4–6 wks)] OR (AMP 12 gm/d IV, continuous or q4h + gent as above x4–6 wks)	Vanco 30 mg/kg/d IV in 2 div. doses to max. of 2 gm/d unless serum levels measured PLUS gentamicin 1 mg/kg q8h IV x4–6 wks

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ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS*	
		PRIMARY	ALTERNATIVE§
Heart, Infective endocarditis—Native valve—culture positive *(continued)*			
Enterococci: MIC streptomycin >2000 μg/ml MIC gentamicin >500–2000 μg/ml No resistance to penicillin	Enterococci, high-level aminoglycoside resistance	Pen G or AMP IV as above x8–12 wks (approx. 50% cure)	If prolonged Pen G/amp fails, consider surgical removal of infected valve
Enterococci: β-lactamase production test is **positive** and **no** gentamicin resistance	Enterococci, penicillin resistance	AM/SB 3.0 gm q6h IV PLUS gentamicin 1 mg/kg q8h IV x4–6 wks	AMP/SB 3.0 gm IV q6h PLUS vanco 30 mg/kg/d IV in 2 div. doses (check levels if >2 gm) x4–6 wks
Enterococci: β-lactamase test neg.; Pen G MIC >16 μg/ml; no gentamicin resistance	Enterococci, intrinsic Pen G/amp resistance	Vanco 30 mg/kg/d IV in 2 div. doses (check levels if >2 gm) PLUS gent. 1 mg/kg q8h (no single dose) x4–6 wks	
Enterococci: Pen/amp resistant PLUS high-level gent/strep resistant PLUS vanco resistant Consultation suggested	Enterococci, vanco-resistant, usually E. faecium	No reliable effective rx. Can try quinupristin + dalfopristin (Synercid)—*see Comment and footnote*[1]	Teicoplanin active against a subset of vanco-resistant enterococci. Teicoplanin is no longer available in U.S.
Staphylococcal endocarditis—aortic and/or mitral valve infection	Staph. aureus, methicillin-sensitive	Nafcillin (oxacillin) 2 gm q4h IV x4–6 wks PLUS gentamicin 1.0 mg/kg q8h IV x3–5 d.	[(Cefazolin 2.0 gm q8h IV x4–6 wks) PLUS (gentamicin 1.0 mg/kg q8h IV x3–5 d.)] OR Vanco 30 mg/kg/d IV in 2 div. doses (check levels if >2 gm/d.) x4–6 wks
Tricuspid valve infection (usually IVDUs)	Staph. aureus, methicillin-sensitive	Nafcillin (oxacillin) 2 gm q4h IV PLUS gentamicin 1 mg/kg q8h IV x2 wks	Nafcillin PLUS gentamicin, *as in Staph. endocarditis, above*

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ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	ALTERNATIVE§
Heart, Infective endocarditis, native valve, culture positive *(continued)*			
Methicillin resistance (MRSA)	Staph. aureus, methicillin-resistant	Vanco 30 mg/kg/d IV in 2 div. doses (check levels if >2 gm/day) x4–6 wks	
Slow-growing fastidious Gm-neg. bacilli	HACEK group *(See Comments) (Mayo Clin Proc 72:532, 1997)*	Ceftriaxone 2.0 gm qd IV x4 wks	AMP 12 gm qd (continuous or div. q4h) x4 wks + gentamicin 1.0 mg/kg q8h IV or IM x4 wks
Infective endocarditis—culture negative			
Fever, valvular disease, and ECHO vegetations ± emboli and neg. cultures	Q fever, psittacosis, brucellosis, bartonella, fungi	Emphasis is on diagnosis. See specific organism for treatment regimens.	
Infective endocarditis—Prosthetic valve—empiric therapy (cultures pending)			
Early (<2 months post-op)	S. epidermidis, S. aureus. Rarely, Enterobacteriaceae, diphtheroids, fungi	Vanco 15 mg/kg q12h IV + gentamicin 1.0 mg/kg q8h IV + RIF 600 mg po daily	
Late (>2 months post-op)	S. epidermidis, S. viridans, enterococci, S. aureus		
Infective endocarditis—Prosthetic valve—positive blood cultures	Staph. epidermidis	(Vanco 15 mg/kg q12h IV + RIF 300 mg q8h po) x6 wks + gentamicin 1.0 mg q8h IV x14 d.	
Surgical consultation advised	Staph. aureus	Methicillin sensitive: (Nafcillin 2.0 gm q4h IV + RIF 30 Methicillin resistant: (Vanco 1.0 gm q12h IV + RIF 30	+ gent x 14 d
	Strep. viridans, enterococci	*As for Native valve, above*	
	Enterobacteriaceae or P. aeruginosa	APAG (tobramycin if P. aeruginosa) + (AP Pen or P Ceph 3 AP or P Ceph 4)	
	Candida, aspergillus	Amphotericin B ± an azole, e.g., fluconazole *(Table 11, page 72)*	
Pericarditis, purulent	Staph. aureus, Strep. pneumoniae, Group A strep, Enterobacteriaceae	PRSP + APAG *(Dosage, see footnote)*[1]	IMP or TC/CL or PIP/TZ or AM/SB or MER or CFP *(see footnote)*[1]
Rheumatic fever *See Ln 349:935, 1997* *Also see Table 15, pages 111,114*	Post-infectious sequelae of Group A strep infection (usually pharyngitis)	Salicylates	Corticosteroids

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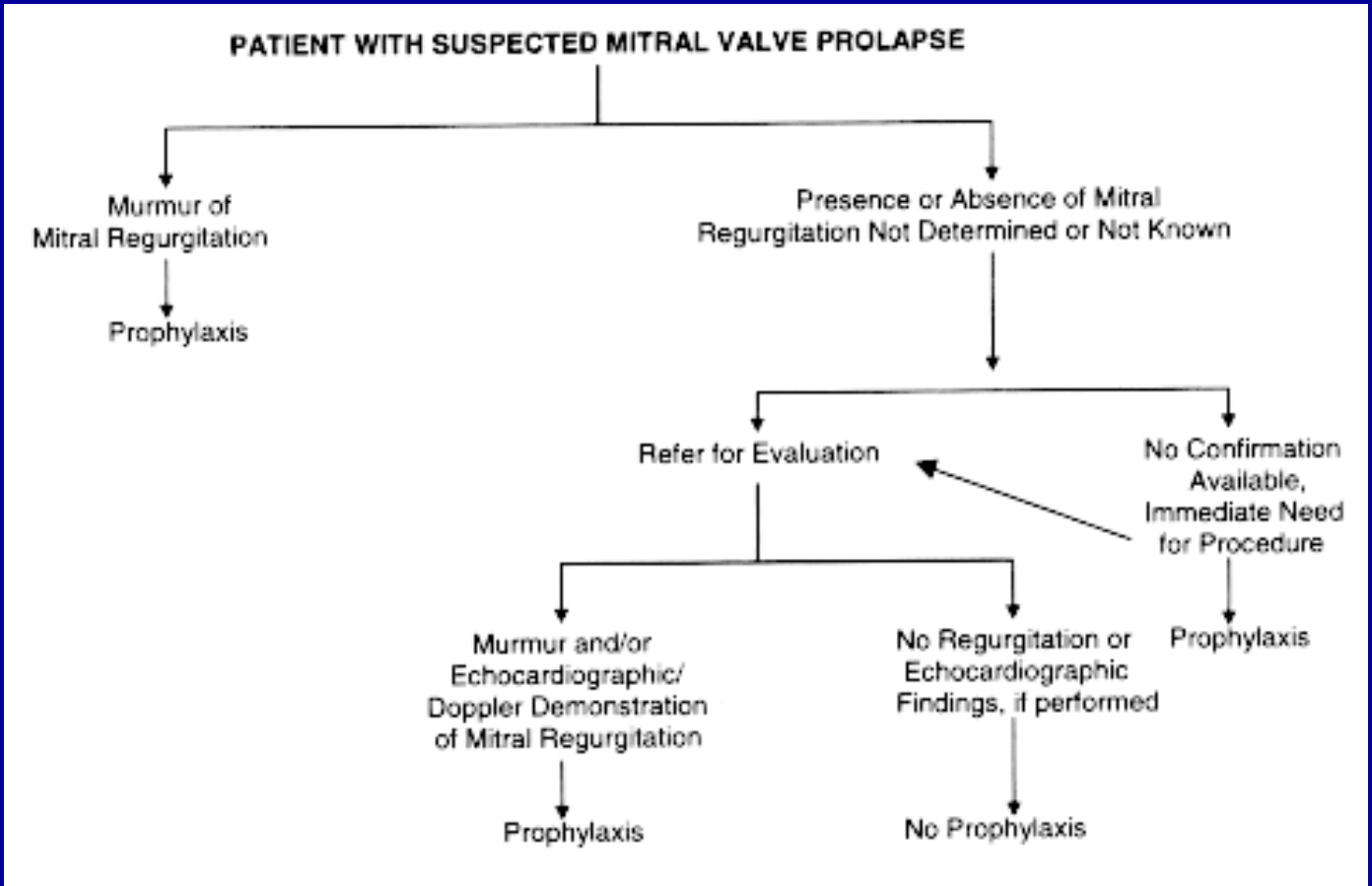
Surgery for PVE

	Indication	Class
1.	Early prosthetic valve endocarditis (first 2 months or less after surgery).	I
2.	Heart failure with prosthetic valve dysfunction.	I
3.	Fungal endocarditis.	I
4.	Staphylococcal endocarditis not responding to antibiotic therapy.	I
5.	Evidence of paravalvular leak, annular or aortic abscess, sinus or aortic true or false aneurysm, fistula formation, or new-onset conduction disturbances.	I
6.	Infection with gram-negative organisms or organisms with a poor response to antibiotics.	I
7.	Persistent bacteremia after a prolonged course (7 to 10 days) of appropriate antibiotic therapy without noncardiac causes for bacteremia.	IIa
8.	Recurrent peripheral embolus despite therapy.	IIa
9.	Vegetation of any size on or near the prosthesis.	IIb

*Criteria exclude repaired mitral valves or aortic allograft or autograft valves. Endocarditis is defined by clinical criteria with or without laboratory verification.

IE Prophylaxis in MVP



Antibiotic Prophylaxis

Situation	Agent	Regimen
Standard general prophylaxis	Amoxicillin	Adults: 2.0 g; children: 50 mg/kg orally 1 h before procedure
Unable to take oral medications	Ampicillin	Adults: 2.0 g IM or IV; children: 50 mg/kg IM or IV within 30 min before procedure
Allergic to penicillin	Clindamycin **or**	Adults: 600 mg; children: 20 mg/kg orally 1 h before procedure
	Cephalexin† or cefadroxil† **or**	Adults: 2.0 g; children; 50 mg/kg orally 1 h before procedure
	Azithromycin or clarithromycin	Adults: 500 mg; children: 15 mg/kg orally 1 h before procedure
Allergic to penicillin and unable to take oral medications	Clindamycin **or**	Adults: 600 mg; children: 20 mg/kg IV within 30 min before procedure
	Cefazolin†	Adults: 1.0 g; children: 25 mg/kg IM or IV within 30 min before procedure

IM indicates intramuscularly, and IV, intravenously.
*Total children's dose should not exceed adult dose.
†Cephalosporins should not be used in individuals with immediate-type hypersensitivity reaction (urticaria, angioedema, or anaphylaxis) to penicillins.

Antibiotic Prophylaxis

Situation	Agents*	Regimen†
High-risk patients	Ampicillin plus gentamicin	Adults: ampicillin 2.0 g IM or IV plus gentamicin 1.5 mg/kg (not to exceed 120 mg) within 30 min of starting procedure; 6 h later, ampicillin 1 g IM/IV or amoxicillin 1 g orally
		Children: ampicillin 50 mg/kg IM or IV (not to exceed 2.0 g) plus gentamicin 1.5 mg/kg within 30 min of starting the procedure; 6 h later, ampicillin 25 mg/kg IM/IV or amoxicillin 25 mg/kg orally
High-risk patients allergic to ampicillin/amoxicillin	Vancomycin plus gentamicin	Adults: vancomycin 1.0 g IV over 1-2 h plus gentamicin 1.5 mg/kg IV/IM (not to exceed 120 mg); complete injection/infusion within 30 min of starting procedure
		Children: vancomycin 20 mg/kg IV over 1-2 h plus gentamicin 1.5 mg/kg IV/IM; complete injection/infusion within 30 min of starting procedure
Moderate-risk patients	Amoxicillin or ampicillin	Adults: amoxicillin 2.0 g orally 1 h before procedure, or ampicillin 2.0 g IM/IV within 30 min of starting procedure
		Children: amoxicillin 50 mg/kg orally 1 h before procedure, or ampicillin 50 mg/kg IM/IV within 30 min of starting procedure
Moderate-risk patients allergic to ampicillin/amoxicillin	Vancomycin	Adults: vancomycin 1.0 g IV over 1-2 h complete infusion within 30 min of starting procedure
		Children: vancomycin 20 mg/kg IV over 1-2 h; complete infusion within 30 min of starting procedure

IM indicates intramuscularly, and IV, intravenously.
*Total children's dose should not exceed adult dose.
†No second dose of vancomycin or gentamicin is recommended.